



## CLN3 disease

CLN3 disease is an inherited disorder that primarily affects the nervous system. After 4 to 6 years of normal development, children with this condition develop vision impairment, intellectual disability, movement problems, speech difficulties, and seizures, which worsen over time.

In children with CLN3 disease, problems with vision often begin between the ages of 4 and 8 years. Vision impairment worsens with age, and people with CLN3 disease are often blind by late childhood or adolescence. Also around age 4 to 8, children with CLN3 disease start to fall behind in school. They have difficulty learning new information and lose previously acquired skills (developmental regression), usually beginning with loss of the ability to speak in complete sentences.

Movement abnormalities often develop in adolescence in people with CLN3 disease. These abnormalities include muscle rigidity or stiffness, slow or diminished movements (hypokinesia), and a stooped posture. Over time, affected individuals lose the ability to walk or sit independently and require wheelchair assistance. In rare cases, people with CLN3 disease have heart (cardiac) problems, including heart rhythm abnormalities and an increase in the size of the heart muscle (hypertrophic cardiomyopathy). These heart problems usually develop in adolescence or early adulthood. Most people with CLN3 disease live into early adulthood.

CLN3 disease is one of a group of disorders known as neuronal ceroid lipofuscinoses (NCLs), which may also be collectively referred to as Batten disease. All these disorders affect the nervous system and typically cause worsening problems with vision, movement, and thinking ability. The different NCLs are distinguished by their genetic cause. Each disease type is given the designation "CLN," meaning ceroid lipofuscinosis, neuronal, and then a number to indicate its subtype.

### Frequency

CLN3 disease is the most common type of NCL, but its exact prevalence is unknown; more than 400 cases have been described in the scientific literature. Collectively, all forms of NCL affect an estimated 1 in 100,000 individuals worldwide.

### Genetic Changes

CLN3 disease is caused by mutations in the *CLN3* gene, which provides instructions for making a protein called battenin. This protein is primarily located in the membranes surrounding lysosomes and endosomes, which are compartments within the cell that digest and recycle materials. The function of battenin is unclear. Research has shown that this protein has many possible functions, but it is uncertain whether any of these

functions is the primary role of the protein, or if they instead represent downstream effects.

It is unclear how mutations in the *CLN3* gene lead to the characteristic features of CLN3 disease. One *CLN3* gene mutation, found in more than 90 percent of cases, leads to the production of an abnormally short protein that is probably broken down quickly. As a result, there is a severe reduction in the amount of functional battenin in cells. Other mutations also reduce the amount or impair the function of battenin. It is not known how the loss of this protein causes the signs and symptoms of CLN3 disease.

CLN3 disease, like other NCLs, is characterized by the accumulation of proteins and other substances in lysosomes. These accumulations occur in cells throughout the body; however, nerve cells seem to be particularly vulnerable to their effects. The accumulations can cause cell damage leading to cell death. The progressive death of nerve cells in the brain and other tissues leads to the neurological signs and symptoms of CLN3 disease. Additionally, it is thought that cardiac cell damage and death due to lysosomal accumulations contribute to the heart problems in people with CLN3 disease. However, it is unclear how mutations in the *CLN3* gene are involved in the buildup of substances in lysosomes.

## **Inheritance Pattern**

This condition is inherited in an autosomal recessive pattern, which means both copies of the gene in each cell have mutations. The parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition.

## **Other Names for This Condition**

- Batten-Mayou disease
- Batten-Spielmeyer-Vogt disease
- CLN3-related neuronal ceroid-lipofuscinosis
- juvenile Batten disease
- Juvenile cerebroretinal degeneration
- juvenile neuronal ceroid lipofuscinosis
- Spielmeyer-Vogt disease

## **Diagnosis & Management**

### Genetic Testing

- Genetic Testing Registry: Juvenile neuronal ceroid lipofuscinosis  
<https://www.ncbi.nlm.nih.gov/gtr/conditions/C0751383/>

### Other Diagnosis and Management Resources

- Batten Disease Diagnostic and Clinical Research Center at the University of Rochester Medical Center  
<https://www.urmc.rochester.edu/neurology/batten-disease-center.aspx>
- Batten Disease Support and Research Association: Centers of Excellence  
<http://bdsra.org/centers-of-excellence/>
- GeneReview: Neuronal Ceroid-Lipofuscinoses  
<https://www.ncbi.nlm.nih.gov/books/NBK1428>

### General Information from MedlinePlus

- Diagnostic Tests  
<https://medlineplus.gov/diagnostictests.html>
- Drug Therapy  
<https://medlineplus.gov/drugtherapy.html>
- Genetic Counseling  
<https://medlineplus.gov/geneticcounseling.html>
- Palliative Care  
<https://medlineplus.gov/palliativecare.html>
- Surgery and Rehabilitation  
<https://medlineplus.gov/surgeryandrehabilitation.html>

## **Additional Information & Resources**

### MedlinePlus

- Encyclopedia: Neuronal Ceroid Lipofuscinoses  
<https://medlineplus.gov/ency/article/001613.htm>
- Health Topic: Degenerative Nerve Diseases  
<https://medlineplus.gov/degenerativenervediseases.html>

### Genetic and Rare Diseases Information Center

- Neuronal ceroid lipofuscinosis 3  
<https://rarediseases.info.nih.gov/diseases/5897/neuronal-ceroid-lipofuscinosis-3>

### Additional NIH Resources

- National Institute of Neurological Disorders and Stroke: Batten Disease Fact Sheet  
<https://www.ninds.nih.gov/Disorders/All-Disorders/Batten-Disease-Information-Page>
- National Institute of Neurological Disorders and Stroke: Epilepsy Information Page  
<https://www.ninds.nih.gov/Disorders/All-Disorders/Epilepsy-Information-Page>

### Educational Resources

- Disease InfoSearch: Juvenile neuronal ceroid lipofuscinosis  
<http://www.diseaseinfosearch.org/Juvenile+neuronal+ceroid+lipofuscinosis/8699>
- MalaCards: juvenile batten disease  
[http://www.malacards.org/card/juvenile\\_batten\\_disease](http://www.malacards.org/card/juvenile_batten_disease)
- NCL Resource: A Gateway for Batten Disease  
<http://www.ucl.ac.uk/ncl/batten.shtml>
- Orphanet: Juvenile neuronal ceroid lipofuscinosis  
[http://www.orpha.net/consor/cgi-bin/OC\\_Exp.php?Lng=EN&Expert=79264](http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=79264)

### Patient Support and Advocacy Resources

- American Association on Intellectual and Developmental Disabilities (AAIDD)  
<http://aaidd.org/>
- American Foundation for the Blind: What You Need to Know About Low Vision  
<http://www.visionaware.org/info/your-eye-condition/eye-health/low-vision/123>
- Batten Disease Family Association (UK)  
<http://www.bdfa-uk.org.uk/>
- Batten Disease Support and Research Association  
<http://bdsra.org/>
- Beyond Batten Disease Foundation  
<http://beyondbatten.org/>
- National Organization for Rare Disorders (NORD)  
<https://rarediseases.org/rare-diseases/batten-disease/>

### GeneReviews

- Neuronal Ceroid-Lipofuscinoses  
<https://www.ncbi.nlm.nih.gov/books/NBK1428>

### ClinicalTrials.gov

- ClinicalTrials.gov  
<https://clinicaltrials.gov/ct2/results?cond=%22juvenile+Batten+disease%22+OR+%22juvenile+neuronal+ceroid+lipofuscinosis%22+OR+%22Batten+Disease%22+OR+%22Neuronal+Ceroid-Lipofuscinoses%22>

## Scientific Articles on PubMed

- PubMed  
<https://www.ncbi.nlm.nih.gov/pubmed?term=%28Neuronal+Ceroid-Lipofuscinosis%5BMAJR%5D%29+AND+%28%28batten+disease%5BTIAB%5D%29+OR+%28juvenile+NCL%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1800+days%22%5Bdp%5D>

## OMIM

- CEROID LIPOFUSCINOSIS, NEURONAL, 3  
<http://omim.org/entry/204200>

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